

WHAT IS CLAIMED IS:

1. A cloned DNA sequence encoding a polypeptide of hap gene, wherein the sequence has the formula

ATGTTTGACTGTATGGATGTTCTGTCACTGAGTCCTGGGCAAATCCTGATTCTACACTGCGAGTCC
GTCTTCCTGCATGCTCCAGGAGAAAGCTCTCAAAGCATGCTTCAGTGGATTGACCCAAACCGAATG
GCAGCATCGGCACACTGCTCAATCAATTGAAACACAGAGCACCAGCTCTGAGGAACTCGTCCCAAG
CCCCCATCTCCACTTCCTCCCCCTCGAGTGATCAAACCCTGCTTCGTCTGCCAGGACAAATCATC
AGGGTACCACTATGGGGTCAGCGCCTGTGAGGGATGAAGGGCTTTTTCCGCAGAAGTATTCAGAAG
AATATGATTTACACTTGTCACCGAGATAAGAACTGTGTTATTAATAAAGTCACCAGGAATCGATGC
CAATACTGTGACTCCAGAAGTGCTTTGAAGTGGGAATGTCCAAAGAATCTGTCAGGAATGACAGG
AACAAGAAAAAGAAGGAGACTTCGAAGCAAGAATGCACAGAGAGCTATGAAATGACAGCTGAGTTG
GACGATCTCACAGAGAAGATCCGAAAAGCTCACCAGGAACTTTCCTTCACTCTCGCAGCTGGGT
AAATACACCACGAATTCCAGTGCTGACCATCGAGTCCGACTGGACCTGGGCCTCTGGGACAAATTC
AGTGAACCTGGCCACCAAGTGCATTATTAAGATCGTGGAGTTTGCTAAACGTCTGCCTGGTTTCACT
GGCTTGACCATCGCAGACCAAATTACCTGCTGAAGGCCGCTGCCTGGACATCCTGATTCTTAGA
ATTTGCACCAGGTATACCCCAGAACAGACACCATGACTTTCTCAGACGGCCTTACCCTAAATCGA
ACTCAGATGCACAATGCTGGATTTGGTCCTCTGACTGACCTTGTGTTACCTTTGCCAACCAGCTC
CTGCCTTTGGAAATGGATGACACAGAAACAGGCCTTCTCAGTGCCATCTGCTTAATCTGTGGAGAC
CGCCAGGACCTTGAGGAACCGACAAAAGTAGATAAGCTACAAGAACCATTGCTGGAAGCACTAAAA
ATTTATATCAGAAAAAGACGACCCAGCAAGCCTCACATGTTTCCAAAGATCTTAATGAAAATCACA
GATCTCCGTAGCATCAGTGCTAAAGGTGCAGAGCGTGAATTACCTTGAAAATGGAAATTCCTGGA
TCAATGCCACCTCTCATTCAAGAAATGATGGAGAATTCTGAAGGACATGAACCCTTGACCCCAAGT
TCAAGTGGGAACACAGCAGAGCACAGTCCTAGCATCTCACCAGCTCAGTGGAACAGTGGGGTC
AGTCAGTCACCACTCGTGCAATAA,

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cont.

and serotypic variants thereof, wherein said DNA is in a purified form.

2. DNA sequence as claimed in claim 1, which is free of human serum proteins, viral proteins, and nucleotide sequences encoding said proteins.

3. DNA sequence as claimed in claim 1, which is free of human tissue.

4. DNA sequence as claimed in claim ⁵⁷~~1~~, wherein the sequence has the formula:

GTCAGGAATGACAGGAACAAGAAAAAGAAGGAGACTTCGAAGCAAGAATGC.

5. DNA sequence as claimed in claim ⁵⁷~~1~~, wherein the sequence has the formula:

GCTGAGTTGGACCATCTCACAGAGAAGATCCGA.

6. DNA sequence as ⁵⁷~~claimed~~ in claim ⁵⁷~~1~~, wherein the sequence has the formula:

GGGGTCACTCAGTCACCACTCGTGCAA.

7. DNA sequence as ⁵⁷~~claimed~~ in claim ⁵⁷~~1~~, wherein the sequence has the formula:

AATGACAGGAACAAGAAAAAGAAGGAGACT.

8. DNA sequence as ⁵⁷~~claimed~~ in claim ⁵⁷~~1~~, wherein the sequence has the formula:

ATGTTTGACTGTATGGATGTTCTGTCACTGAGTCCTGGGCAAATCCTCGATTTC
TACACTGCGAGTCCGTCTTCCTGCATGCTCCAGGAGAAAGCTCTCAAAGCATGC
TTCAGTGGATTGACCCAAACCGAATGGCAGCATCGGCACACTGCTCAATCA.

9. DNA sequence as ⁵⁷~~claimed~~ in claim ⁵⁷~~1~~, wherein the sequence has the formula:

CATGAACCCTTGACCCCAAGTTCAAGTGGGAACACAGCAGAGCACACTCCTAGC
ATCTCACCCAGCTGAGTGGAAAACAGTGGGGTCACTCAGTCACCACTCGTGCAA.

10. A DNA probe consisting essentially of a radionuclide bonded to the DNA sequence of claim 1.

11. A hybrid duplex molecule consisting essentially of the DNA sequence of claim 1 hydrogen bonded to a nucleotide sequence of complementary base sequence.

12. Hybrid duplex molecule as claimed in claim ¹¹9, wherein said nucleotide sequence is a DNA sequence.

13. Hybrid duplex molecule as claimed in claim ¹¹9, wherein said nucleotide sequence is a RNA sequence.

14. Hybrid duplex molecule as claimed in claim ¹¹9, wherein a radionuclide label is bonded to said DNA sequence.

15. A polypeptide comprising an amino acid sequence of hap protein, wherein the polypeptide contains the amino acid sequence

MetPheAspCysMetAspValLeuSerValSerProGlyGlnIleLeuAspPheTyrThrAla
SerProSerSerCysMetLeuGlnGluLysAlaLeuLysAlaCysPheSerGlyLeuThrGln
ThrGluTrpGlnHisArgHisThrAlaGlnSerIleGluThrGlnSerThrSerSerGluGlu
LeuValProSerProProSerProLeuProProProArgValTyrLysProCysPheValCys
GlnAspLysSerSerGlyTyrHisTyrGlyValSerAlaCysGluGlyCysLysGlyPhePhe
ArgArgSerIleGlnLysAsnMetIleTyrThrCysHisArgAspLysAsnCysValIleAsn
LysValThrArgAspArgCysGlnTyrCysArgLeuGlnLysCysPheGluValGlyMetSer
LysGluSerValArgAsnAspArgAsnLysLysLysLysGluThrSerLysGlnGluCysThr
GluSerTyrGluMetThrAlaGluLeuAspAspLeuThrGluLysIleArgLysAlaHisGln
GluThrPheProSerLeuCysGlnLeuGlyLysTyrThrThrAsnSerSerAlaAspHisArg

ValArgLeuAspLeuGlyLeuTrpAspLysPheSerGluLeuAlaThrLysCysIleIleLys
IleValGluPheAlaLysArgLeuProGlyPheThrGlyLeuThrIleAlaAspGlnIleThr
LeuLeuLysAlaAlaCysLeuAspIleLeuIleLeuArgIleCysThrArgTyrThrProGlu
GlnAspThrMetThrPheSerAspGlyLeuThrLeuAsnArgThrGlnMetHisAsnAlaGly
PheGlyProLeuThrAspLeuValPheThrPheAlaAsnGlnLeuLeuProLeuGluMetAsp
AspThrGluThrGlyLeuLeuSerAlaIleCysLeuIleCysGlyAspArgGlnAspLeuGlu
GluProThrLysValAspLysLeuGlnGluProLeuLeuGluAlaLeuLysIleTyrIleArg
LysArgArgProSerLysProHisMetPheProLysIleLeuMetLysIleThrAspLeuArg
SerIleSerAlaLysGlyAlaGluArgValIleThrLeuLysMetGluIleProGlySerMet
ProProLeuIleGlnGluMetMetGluAsnSerGluGlyHisGluProLeuThrProSerSer
SerGlyAsnThrAlaGluHisSerProSerIleSerProSerSerValGluAsnSerGlyVal
SerGlnSerProLeuValGln,

and serotypic variants and fragments thereof, wherein said poly-
peptide is free from human serum proteins, virus, viral protein,
human tissue, and human tissue components.

16. Polypeptide as claimed in claim 15, which is free from
human, blood-derived protein.

17. A polypeptide as claimed in claim 15, wherein the poly-
peptide comprises a peptide fragment having the amino acid se-
quence:

GlnHisArgHisThrAlaGlnSerIleGluThrGlnSerThrSerSerGluGlu
LeuValProSerProProSerProLeuProProProArgValTyrLysProCysPheValCys
GlnAspLysSerSerGlyTyrHisTyrGlyValSerAlaCysGluGlyCysLysGlyPhePhe
ArgArgSerIleGlnLysAsnMetIleTyrThrCysHisArgAspLysAsnCysValIleAsn

LysValThrArgAsnArgCysGlnTyrCysArgLeuGlnLysCysPheGluValGlyMetSer
LysGluSerValArgAsnAspArgAsnLysLysLysLysGluThrSerLysGlnGluCysThr
GluSerTyrGluMetThrAlaGluLeuAspAspLeuThrGluLysIleArgLysAlaHisGln
GluThrPheProSerLeuCys.

18. A polypeptide as claimed in claim 15, wherein the polypeptide comprises a peptide fragment having the amino acid sequence:

ValArgAsnAspArgAsnLysLysLysLysGluThrSerLysGlnGluCys (peptide 1);
and serotypic variants thereof.

19. A polypeptide as claimed in claim 15, wherein the polypeptide comprises a peptide fragment having the amino acid sequence:

AsnAspArgAsnLysLysLysLysGluThrCys (peptide 2);
and serotypic variants thereof.

20. A polypeptide as claimed in claim 15, wherein the polypeptide comprises a peptide fragment having the amino acid sequence:

CysGlyValSerGlnSerProLeuValGln (peptide 3);
and serotypic variants thereof.

21. A polypeptide as claimed in claim 15, wherein the polypeptide comprises a peptide fragment having the amino acid sequence:

AlaGluLeuAspAspLeuThrGluLysIleArg;

and serotypic variants thereof.

22. A polypeptide as claimed in claim 15, wherein the polypeptide comprises a peptide fragment having the amino acid sequence:

MetPheAspCysMetAspValLeuSerValSerProGlyGlnIleLeuAspPheTyrThr
AlaSerProSerSerCysMetLeuGlnGluLysAlaLeuLysAlaCysPheSerGlyLeu
ThrGlnThrGluTrpGlnHisArgHisThrAlaGlnSer.

23. A polypeptide as claimed in claim 15, wherein the polypeptide comprises a peptide fragment having the amino acid sequence:

HisGluProLeuThrProSerSerSerGlyAsnThrAlaGluHisSerProSer
IleSerProSerSerValGluAsnSerGlyValSerGlnSerProLeuValGln

24. A process for selecting a nucleotide sequence coding for hap protein or a portion thereof from a group of nucleotide sequences comprising the step of determining which of said nucleotide sequences hybridizes to a DNA sequence as claimed in claim 1.

25. Process as claimed in claim ²⁴/₂₀, wherein said nucleotide sequence is a DNA sequence.

26. Process as claimed in claim ²⁵/₂₁, wherein said nucleotide sequence is selected by Southern blot technique.

C 27. Process as claimed in claim ²⁴20, wherein said nucleotide sequence is a RNA sequence.

C 28. Process as claimed in claim ²⁷23, wherein said nucleotide sequence is selected by Northern blot technique.

C 29. Process as claimed in claim ²⁴20, wherein said process comprises the step of detecting a label bonded to said DNA sequence.

C 30. Process as claimed in claim ²⁹25, wherein said label is a radionuclide.

31. A recombinant vector comprising lambda-NM1149 having an EcoRI restriction endonuclease site into which has been inserted the DNA sequence as claimed in claim 1.

32. Plasmid pCOD20.

C 33. An E. coli bacterial culture in a purified form, wherein the culture comprises E. coli cells containing ^{a plasmid}DNA, wherein a portion of said ^{plasmid}DNA comprises the DNA sequence as claimed in claim 1.

C 34. Bacterial culture as claimed in claim 27, wherein said cells are comprised of E. coli strain TG-1.

35. A method for assaying a fluid for the presence of an agonist or antagonist to retinoic acid receptor RAR- β , wherein the method comprises

(A) providing an aqueous solution containing a known concentration of the proteinaceous receptor as claimed in claim 13;

(B) incubating the receptor with the fluid suspected of containing the agonist or antagonist under conditions sufficient to bind the receptor to the agonist or antagonist; and

(C) determining whether there is change in concentration of the proteinaceous receptor in the aqueous solution.

36. Method as claimed in claim 35, wherein the receptor and the agonist or antagonist form a complex.

37. Method as claimed in claim 36, wherein a crosslinking agent is present in an amount sufficient to inhibit dissociation of the receptor and the agonist or antagonist.

38. A cloned DNA sequence encoding a polypeptide of hap gene, wherein the sequence has the formula

CCCATGC

GAGCTGTTTGAAGGACTGGGATGCCGAGAACGCGAGCGATCCGAGCAGGGTTTGTCTGGGCACCGT
ATGTTTGACTGTATGGATGTTCTGTCACTGAGTCCTGGGCAAATCCTGATTCTACACTGCGAGTCC
GTCTTCCTGCATGCTCCAGGAGAAAGCTCTCAAAGCATGCTTCAGTGGATTGACCCAAACCGAATG
GCAGCATCGGCACACTGCTCAATCAATTGAAACACAGAGCACCAGCTCTGAGGAACTCGTCCCAAG
CCCCCATCTCCACTTCCTCCCCCTCGAGTGATCAAACCCTGCTTCGTCTGCCAGGACAAATCATC
AGGGTACCACTATGGGGTCAGCGCCTGTGAGGATGAAGGGCTTTTTCCGCAGAAGTATTCAGAAG
AATATGATTTACACTTGTCACCGAGATAAGAAGTGTGTTATTAATAAAGTCACCAGGAATCGATGC
CAATACTGTCTGACTCCAGAAGTGCTTTGAAGTGGGAATGTCCAAAGAATCTGTCAGGAATGACAGG
AACAAGAAAAAGAAGGAGACTTCGAAGCAAGAATGCACAGAGAGCTATGAAATGACAGCTGAGTTG
GACGATCTCACAGAGAAGATCCGAAAAGCTCACCAGGAACTTTCCCTTCACTCTCGCAGCTGGGT
AAATACACCACGAATTCAGTGCTGACCATCGAGTCCGACTGGACCTGGGCCTCTGGGACAAATTC
AGTGAAGTGGCCACCAAGTGCATTATTAAGATCGTGGAGTTTGCTAAACGTCTGCCTGGTTTCACT
GGCTTGACCATCGCAGACCAAATTACCCTGCTGAAGGCCGCTGCCTGGACATCCTGATTCTTAGA
ATTTGCACCAGGTATACCCAGAACAAAGACACCATGACTTTCTCAGACGGCCTTACCCTAAATCGA
ACTCAGATGCACAATGCTGGATTTGGTCCTCTGACTGACCTTGTTTACCTTTGCCAACCAGCTC

CTGCCTTTGGAAATGGATGACACAGAAACAGGCCTTCTCAGTGCCATCTGCTTAATCTGTGGAGAC
CGCCAGGACCTTGAGGAACCCACAAAAGTAGATAAGCTACAAGAACCATTGCTGGAAGCACTAAAA
ATTTATATCAGAAAAAGACGACCCAGCAAGCCTCACATGTTTCCAAAGATCTTAATGAAAATCACA
GATCTCCGTAGCATCAGTGCTAAAGGTGCAGAGCGTGTAATTACCTTGAAAATGGAAATTCCTGGA
TCAATGCCACCTCTCATTCAAGAAATGATGGAGAATTCTGAAGGACATGAACCCTTGACCCCAAGT
TCAAGTGGGAACACAGCAGAGCACAGTCCCTAGCATCTCACCCAGCTCAGTGGAAAACAGTGGGGTC
AGTCAGTCACCACTCGTGCAATAA,

and serotypic variants thereof, wherein said DNA is in a purified form.

39. ^a DNA sequence as claimed in claim ⁵⁹~~38~~, which is free of human serum proteins, viral proteins, and nucleotide sequences encoding said proteins.

40. ^a DNA sequence as claimed in claim 1, which is free of human tissue.

41. A DNA probe consisting essentially of a radionuclide bonded to the DNA sequence of claim ⁵⁹~~38~~.

42. A hybrid duplex molecule consisting essentially of the DNA sequence of claim ⁵⁹~~38~~ hydrogen bonded to a nucleotide sequence of complementary base sequence.

43. Hybrid duplex molecule as claimed in claim 11, wherein said nucleotide sequence is a DNA sequence.

44. Hybrid duplex molecule as claimed in claim 11, wherein said nucleotide sequence is a RNA sequence.

45. Hybrid duplex molecule as claimed in claim 11, wherein a radionuclide label is bonded to said DNA sequence.

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46. A process for selecting a nucleotide sequence coding for hap protein or a portion thereof from a group of nucleotide sequences comprising the step of determining which of said nucleotide sequences hybridizes to a DNA sequence as claimed in claim 38.

C
47. Process as claimed in claim ⁴⁶~~24~~, wherein said nucleotide sequence is a DNA sequence.

C
48. Process as claimed in claim ⁴⁷~~24~~, wherein said nucleotide sequence is selected by Southern blot technique.

49. Process as claimed in claim 46, wherein said nucleotide sequence is a RNA sequence.

C
50. Process as claimed in claim ⁴⁸~~46~~, wherein said nucleotide sequence is selected by Northern blot technique.

51. Process as claimed in claim 46, wherein said process comprises the step of detecting a label bonded to said DNA sequence.

52. Process as claimed in claim 51, wherein said label is a radionuclide.

53. A recombinant DNA molecule comprising a DNA sequence of coding for a retinoic acid receptor, said DNA sequence coding on expression in a unicellular host for a polypeptide displaying the retinoic acid and DNA binding properties of RAR-8 and being operatively linked to an expression control sequence in said DNA molecule. ✓

54. Plasmid pPROHAP. ✓

55. An E. coli bacterial culture in a purified form, where-
in the culture comprises E. coli cells containing ^{a plasmid} ~~DNA~~, wherein a
portion of said ^{plasmid} ~~DNA~~ comprises the DNA sequence as claimed in
claim ⁵ ~~38~~.

56. Bacterial culture as claimed in claim 55, wherein said
cells are comprised of E. coli strain DH5 α F'.

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